

WHAT IS CLAIMED IS:

- 1.** A method of detecting a target mRNA in a cell, the method comprising:
 - (a) providing a labeled RNA, the labeled RNA comprising
 - (i) an RNA comprising at least one double-stranded region, the double-stranded region comprising a sense strand and an antisense strand, the antisense strand comprising a region which is substantially complementary to a region of the target mRNA, and
 - (ii) at least one label;
 - (b) introducing the labeled RNA into the cell, whereby the labeled RNA initiates RNA interference of the target mRNA, which results in an initiation-dependent change in a signal output of the label; and,
 - (c) detecting the signal output, whereby the signal output provides an indication of the presence of the target mRNA in the cell.
- 2.** The method of claim 1, wherein the label is a fluorescent label, wherein the initiation-dependent change in the signal output of the label is a change in fluorescent emission, and wherein detecting the signal output comprises measuring the intensity of the fluorescent emission, whereby the intensity of the fluorescent emission provides an indication of the quantity of the target mRNA present in the cell.
- 3.** The method of claim 2, wherein the labeled RNA comprises at least one quencher, wherein the label and the quencher are positioned in the RNA such that fluorescent emission by the label is quenched by the quencher, wherein initiation of RNA interference by the labeled RNA results in unquenching of the label, and wherein the initiation-dependent change in the signal output is an increase in the fluorescent emission by the label.
- 4.** The method of claim 2, wherein the labeled RNA comprises two fluorescent labels, one being a donor and the other being an acceptor; wherein the donor and acceptor are positioned within the RNA such that energy transfer occurs between them; wherein initiation of RNA interference by the labeled RNA results in loss of energy transfer between the donor and the acceptor; and wherein the initiation-dependent change in the signal output is a decrease in fluorescent emission by the acceptor following excitation of the donor.

- 5.** The method of claim 1, wherein the RNA comprises a first polyribonucleotide comprising the sense strand and a second polyribonucleotide comprising the antisense strand.
- 6.** The method of claim 5, wherein the first polyribonucleotide comprises between 19 and 25 nucleotides, the second polyribonucleotide comprises between 19 and 25 nucleotides, and the double-stranded region comprises between 19 and 25 base pairs.
- 7.** The method of claim 6, wherein the first polyribonucleotide and the second polyribonucleotide each comprise a two nucleotide TT 3' overhang, or wherein the first polyribonucleotide and the second polyribonucleotide form a duplex over their entire length.
- 8.** The method of claim 6, wherein at least one caging group is covalently attached to a 5' hydroxyl or a 5' phosphate of the second polyribonucleotide.
- 9.** The method of claim 6, wherein the label is a fluorescent label, wherein the labeled RNA comprises at least one quencher, wherein the label and the quencher are positioned in the RNA such that fluorescent emission by the label is quenched by the quencher, wherein initiation of RNA interference by the labeled RNA results in unquenching of the label, wherein the initiation-dependent change in the signal output is an increase in the fluorescent emission by the label, and wherein the label is attached to the first polyribonucleotide and the quencher is attached to the second polyribonucleotide, or the label is attached to the second polyribonucleotide and the quencher is attached to the first polyribonucleotide.
- 10.** The method of claim 9, wherein:
one of the label and the quencher is located within three nucleotides of the 3' end of the first polyribonucleotide and the other of the label and the quencher is located within three nucleotides of the 3' end of the second polyribonucleotide;
one of the label and the quencher is located within three nucleotides of the 3' end of the first polyribonucleotide and the other of the label and the quencher is located within three nucleotides of the 5' end of the second polyribonucleotide;
one of the label and the quencher is located within three nucleotides of the 5' end of the first polyribonucleotide and the other of the label and the quencher is located within three nucleotides of the 3' end of the second polyribonucleotide;

one of the label and the quencher is located within three nucleotides of the 5' end of the first polyribonucleotide and the other of the label and the quencher is located within three nucleotides of the 5' end of the second polyribonucleotide;

one of the label and the quencher is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the first polyribonucleotide, and the other of the label and the quencher is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the second polyribonucleotide;

one of the label and the quencher is located within three nucleotides of the 5' end or the 3' end of the first or second polyribonucleotide and the other of the label and the quencher is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the opposite polyribonucleotide;

the label is attached at the 3' end of the first polyribonucleotide and the quencher is attached at the 3' end of the second polyribonucleotide;

the quencher is attached at the 3' end of the first polyribonucleotide and the label is attached at the 3' end of the second polyribonucleotide; or,

one of the label and the quencher is attached at the 5' end of the first polyribonucleotide and the other of the label and the quencher is attached at the 3' end of the second polyribonucleotide.

11. The method of claim **6**, wherein the labeled RNA comprises two fluorescent labels, one being a donor and the other being an acceptor; wherein the donor and acceptor are positioned within the RNA such that energy transfer occurs between them; wherein initiation of RNA interference by the labeled RNA results in loss of energy transfer between the donor and the acceptor; and wherein the donor is attached to the first polyribonucleotide and the acceptor is attached to the second polyribonucleotide, or the donor is attached to the second polyribonucleotide and the acceptor is attached to the first polyribonucleotide.

12. The method of claim **11**, wherein:

one of the donor and the acceptor is located within three nucleotides of the 3' end of the first polyribonucleotide and the other of the donor and the acceptor is located within three nucleotides of the 3' end of the second polyribonucleotide;

one of the donor and the acceptor is located within three nucleotides of the 3' end of the first polyribonucleotide and the other of the donor and the acceptor is located within three nucleotides of the 5' end of the second polyribonucleotide;

one of the donor and the acceptor is located within three nucleotides of the 5' end of the first polyribonucleotide and the other of the donor and the acceptor is located within three nucleotides of the 3' end of the second polyribonucleotide;

one of the donor and the acceptor is located within three nucleotides of the 5' end of the first polyribonucleotide and the other of the donor and the acceptor is located within three nucleotides of the 5' end of the second polyribonucleotide;

one of the donor and the acceptor is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the first polyribonucleotide, and the other of the donor and the acceptor is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the second polyribonucleotide;

one of the donor and the acceptor is located within three nucleotides of the 5' end or the 3' end of the first or second polyribonucleotide and the other of the donor and the acceptor is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the opposite polyribonucleotide;

the donor is attached at the 3' end of the first polyribonucleotide and the acceptor is attached at the 3' end of the second polyribonucleotide;

the acceptor is attached at the 3' end of the first polyribonucleotide and the donor is attached at the 3' end of the second polyribonucleotide; or,

one of the donor and the acceptor is attached at the 5' end of the first polyribonucleotide and the other of the donor and the acceptor is attached at the 3' end of the second polyribonucleotide.

13. The method of claim 1, wherein the RNA comprises a self-complementary polyribonucleotide.

14. The method of claim 1, wherein the double-stranded region comprises fewer than about 25 base pairs, fewer than about 30 base pairs, fewer than about 50 base pairs, fewer than about 80 base pairs, fewer than about 150 base pairs, fewer than about 250 base pairs, fewer than about 500 base pairs, fewer than about 1000 base pairs, or fewer than about 1500 base pairs.

15. The method of claim 1, wherein the labeled RNA comprises one or more first caging groups associated with the RNA, the first caging groups inhibiting the RNA from initiating RNA interference of the target mRNA in the cell; the method comprising initiating RNA interference of the target mRNA by exposing the cell to uncaging energy of a first type, whereby exposure to the uncaging energy frees the RNA from inhibition by the first caging groups.

16. The method of claim 15, wherein the first caging groups inhibit the RNA from initiating RNA interference of the target mRNA by at least about 30%, at least about 50%, at least about 75%, at least about 90%, at least about 95%, or at least about 98%, as compared to the RNA in the absence of the first caging groups.

17. The method of claim 15, wherein the first caging groups prevent the RNA from initiating RNA interference of the target mRNA.

18. The method of claim 15, wherein removal of or an induced conformational change in the first caging groups permits the RNA to initiate RNA interference of the target mRNA.

19. The method of claim 15, wherein the one or more first caging groups associated with the RNA are covalently attached to the RNA.

20. The method of claim 19, wherein the RNA comprises a first polyribonucleotide comprising the sense strand and a second polyribonucleotide comprising the antisense strand, and wherein the first caging group is covalently attached to the first polyribonucleotide and to the second polyribonucleotide.

21. The method of claim 20, wherein the first caging group is attached to the 3' end of the first polyribonucleotide and to the 5' end of the second polyribonucleotide.

22. The method of claim 15, wherein the one or more first caging groups are photoactivatable or photolabile, wherein exposing the cell to uncaging energy of the first type comprises exposing the cell to light of a first wavelength.

23. The method of claim 15, comprising contacting the cell and a test compound, and wherein the cell is exposed to the uncaging energy at a preselected time point with respect to a time at which the cell and the test compound are contacted.

24. The method of claim **15**, wherein the uncaging energy is directed at a preselected subset of a cell population comprising the cell.

25. The method of claim **1**, wherein the labeled RNA comprises a cellular delivery module that can mediate introduction of the labeled RNA into the cell, the cellular delivery module being associated with the RNA, and wherein introducing the labeled RNA into the cell comprises contacting the cell with the labeled RNA associated with the cellular delivery module.

26. The method of claim **25**, wherein the cellular delivery module comprises a polypeptide, a PEP-1 peptide, an amphipathic peptide, an MPG^{ΔNLS} peptide, a cationic peptide, a homopolymer of D-arginine, a homopolymer of histidine, a homopolymer of lysine, a protein transduction domain, a protein transduction domain derived from an HIV-1 Tat protein, from a herpes simplex virus VP22 protein, or from a Drosophila antennapedia protein, a model protein transduction domain, or a model protein transduction domain comprising a homopolymer of D-arginine.

27. The method of claim **25**, wherein the cellular delivery module is covalently attached to the RNA.

28. The method of claim **27**, wherein the RNA comprises a first polyribonucleotide comprising the sense strand and a second polyribonucleotide comprising the antisense strand, and wherein the cellular delivery module is covalently attached to the second polyribonucleotide.

29. The method of claim **27**, wherein the cellular delivery module is attached to the RNA through a disulfide bond; or wherein the covalent attachment between the cellular delivery module and the RNA is reversible by exposure to light of a preselected wavelength, the method comprising exposing the cell to light of the preselected wavelength.

30. The method of claim **27**, wherein the cellular delivery module comprises a lipid or one or more myristoyl groups.

31. The method of claim **25**, wherein the labeled RNA comprises one or more second caging groups associated with the cellular delivery module, the second caging groups

inhibiting the cellular delivery module from mediating introduction of the labeled RNA into the cell; the method comprising initiating introduction of the labeled RNA into the cell by exposing the labeled RNA to uncaging energy of a second type, whereby exposure to the uncaging energy frees the cellular delivery module from inhibition by the second caging groups.

32. The method of claim 1, comprising stimulating the cell.

33. The method of claim 32, wherein stimulating the cell comprises adding a test compound.

34. The method of claim 32, wherein detecting the signal output comprises detecting the signal output at a plurality of time points with respect to a time at which the cell is stimulated.

35. The method of claim 1, wherein detecting the signal output comprises measuring an intensity of the signal output, whereby the intensity of the signal output provides an indication of the quantity of the target mRNA present in the cell, whereby the quantity of the target mRNA present in the cell provides an indication of the efficiency with which the labeled RNA reduces expression of the target mRNA.

36. A kit for detecting a target mRNA in a cell, the kit comprising:

(a) a labeled RNA, the labeled RNA comprising

(i) an RNA comprising at least one double-stranded region, the double-stranded region comprising a sense strand and an antisense strand, the antisense strand comprising a region which is substantially complementary to a region of the target mRNA, and

(ii) at least one label, wherein initiation of RNA interference of the target mRNA by the labeled RNA in the cell results in an initiation-dependent change in a signal output of the label; and,

(b) instructions for using the labeled RNA to detect the presence of the target mRNA in the cell; packaged in one or more containers.

37. The kit of claim 36, wherein the label is a fluorescent label, and wherein the initiation-dependent change in the signal output of the label is a change in fluorescent emission.

38. The kit of claim **37**, wherein the labeled RNA comprises at least one quencher, wherein the label and the quencher are positioned in the RNA such that fluorescent emission by the label is quenched by the quencher, wherein initiation of RNA interference by the labeled RNA results in unquenching of the label, and wherein the initiation-dependent change in the signal output is an increase in the fluorescent emission by the label.

39. The kit of claim **37**, wherein the labeled RNA comprises two fluorescent labels, one being a donor and the other being an acceptor; wherein the donor and acceptor are positioned within the RNA such that energy transfer occurs between them; wherein initiation of RNA interference by the labeled RNA results in loss of energy transfer between the donor and the acceptor; and wherein the initiation-dependent change in the signal output is a decrease in fluorescent emission by the acceptor following excitation of the donor.

40. The kit of claim **36**, wherein the RNA comprises a first polyribonucleotide comprising the sense strand and a second polyribonucleotide comprising the antisense strand.

41. The kit of claim **37**, wherein the first polyribonucleotide comprises between 19 and 25 nucleotides, the second polyribonucleotide comprises between 19 and 25 nucleotides, and the double-stranded region comprises between 19 and 25 base pairs.

42. The kit of claim **41**, wherein the first polyribonucleotide and the second polyribonucleotide each comprise a two nucleotide TT 3' overhang, or wherein the first polyribonucleotide and the second polyribonucleotide form a duplex over their entire length.

43. The kit of claim **41**, wherein at least one caging group is covalently attached to a 5' hydroxyl or a 5' phosphate of the second polyribonucleotide.

44. The kit of claim **41**, wherein the label is a fluorescent label, wherein the labeled RNA comprises at least one quencher, wherein the label and the quencher are positioned in the RNA such that fluorescent emission by the label is quenched by the quencher, wherein initiation of RNA interference by the labeled RNA results in unquenching of the label, wherein the initiation-dependent change in the signal output is an increase in the fluorescent emission by the label, and wherein the label is attached to the first polyribonucleotide and

the quencher is attached to the second polyribonucleotide, or the label is attached to the second polyribonucleotide and the quencher is attached to the first polyribonucleotide.

45. The kit of claim **44**, wherein:

one of the label and the quencher is located within three nucleotides of the 3' end of the first polyribonucleotide and the other of the label and the quencher is located within three nucleotides of the 3' end of the second polyribonucleotide;

one of the label and the quencher is located within three nucleotides of the 3' end of the first polyribonucleotide and the other of the label and the quencher is located within three nucleotides of the 5' end of the second polyribonucleotide;

one of the label and the quencher is located within three nucleotides of the 5' end of the first polyribonucleotide and the other of the label and the quencher is located within three nucleotides of the 3' end of the second polyribonucleotide;

one of the label and the quencher is located within three nucleotides of the 5' end of the first polyribonucleotide and the other of the label and the quencher is located within three nucleotides of the 5' end of the second polyribonucleotide;

one of the label and the quencher is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the first polyribonucleotide, and the other of the label and the quencher is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the second polyribonucleotide;

one of the label and the quencher is located within three nucleotides of the 5' end or the 3' end of the first or second polyribonucleotide and the other of the label and the quencher is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the opposite polyribonucleotide;

the label is attached at the 3' end of the first polyribonucleotide and the quencher is attached at the 3' end of the second polyribonucleotide;

the quencher is attached at the 3' end of the first polyribonucleotide and the label is attached at the 3' end of the second polyribonucleotide; or,

one of the label and the quencher is attached at the 5' end of the first polyribonucleotide and the other of the label and the quencher is attached at the 3' end of the second polyribonucleotide.

46. The kit of claim **41**, wherein the labeled RNA comprises two fluorescent labels, one being a donor and the other being an acceptor; wherein the donor and acceptor are positioned within the RNA such that energy transfer occurs between them; wherein initiation of RNA interference by the labeled RNA results in loss of energy transfer between the donor and the acceptor; and wherein the donor is attached to the first polyribonucleotide and the acceptor is attached to the second polyribonucleotide, or the donor is attached to the second polyribonucleotide and the acceptor is attached to the first polyribonucleotide.

47. The kit of claim **46**, wherein:

one of the donor and the acceptor is located within three nucleotides of the 3' end of the first polyribonucleotide and the other of the donor and the acceptor is located within three nucleotides of the 3' end of the second polyribonucleotide;

one of the donor and the acceptor is located within three nucleotides of the 3' end of the first polyribonucleotide and the other of the donor and the acceptor is located within three nucleotides of the 5' end of the second polyribonucleotide;

one of the donor and the acceptor is located within three nucleotides of the 5' end of the first polyribonucleotide and the other of the donor and the acceptor is located within three nucleotides of the 3' end of the second polyribonucleotide;

one of the donor and the acceptor is located within three nucleotides of the 5' end of the first polyribonucleotide and the other of the donor and the acceptor is located within three nucleotides of the 5' end of the second polyribonucleotide;

one of the donor and the acceptor is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the first polyribonucleotide, and the other of the donor and the acceptor is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the second polyribonucleotide;

one of the donor and the acceptor is located within three nucleotides of the 5' end or the 3' end of the first or second polyribonucleotide and the other of the donor and the acceptor is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the opposite polyribonucleotide;

the donor is attached at the 3' end of the first polyribonucleotide and the acceptor is attached at the 3' end of the second polyribonucleotide;

the acceptor is attached at the 3' end of the first polyribonucleotide and the donor is attached at the 3' end of the second polyribonucleotide; or,

one of the donor and the acceptor is attached at the 5' end of the first polyribonucleotide and the other of the donor and the acceptor is attached at the 3' end of the second polyribonucleotide.

48. The kit of claim **36**, wherein the RNA comprises a self-complementary polyribonucleotide.

49. The kit of claim **36**, wherein the double-stranded region comprises fewer than about 25 base pairs, fewer than about 30 base pairs, fewer than about 50 base pairs, fewer than about 80 base pairs, fewer than about 150 base pairs, fewer than about 250 base pairs, fewer than about 500 base pairs, fewer than about 1000 base pairs, or fewer than about 1500 base pairs.

50. The kit of claim **36**, wherein the labeled RNA comprises one or more first caging groups associated with the RNA, the first caging groups inhibiting the RNA from initiating RNA interference of the target mRNA in the cell.

51. The kit of claim **50**, wherein the first caging groups inhibit the RNA from initiating RNA interference of the target mRNA by at least about 30%, at least about 50%, at least about 75%, at least about 90%, at least about 95%, or at least about 98%, as compared to the RNA in the absence of the first caging groups, or wherein the first caging groups prevent the RNA from initiating RNA interference of the target mRNA.

52. The kit of claim **50**, wherein removal of or an induced conformational change in the first caging groups permits the RNA to initiate RNA interference of the target mRNA.

53. The kit of claim **50**, wherein the one or more first caging groups associated with the RNA are covalently attached to the RNA.

54. The kit of claim **53**, wherein the RNA comprises a first polyribonucleotide comprising the sense strand and a second polyribonucleotide comprising the antisense strand, and wherein the first caging group is covalently attached to the first polyribonucleotide and to the second polyribonucleotide.

55. The kit of claim **54**, wherein the first caging group is attached to the 3' end of the first polyribonucleotide and to the 5' end of the second polyribonucleotide.

56. The kit of claim **50**, wherein the one or more first caging groups are photoactivatable or photolabile.

57. The kit of claim **36**, wherein the labeled RNA comprises a cellular delivery module that can mediate introduction of the labeled RNA into the cell, the cellular delivery module being associated with the RNA.

58. The kit of claim **57**, wherein the cellular delivery module comprises a polypeptide, a PEP-1 peptide, an amphipathic peptide, an MPG^{ΔNLS} peptide, a cationic peptide, a homopolymer of D-arginine, a homopolymer of histidine, a homopolymer of lysine, a protein transduction domain, a protein transduction domain derived from an HIV-1 Tat protein, from a herpes simplex virus VP22 protein, or from a Drosophila antennapedia protein, a model protein transduction domain, or a model protein transduction domain comprising a homopolymer of D-arginine.

59. The kit of claim **57**, wherein the cellular delivery module is covalently attached to the RNA.

60. The kit of claim **59**, wherein the RNA comprises a first polyribonucleotide comprising the sense strand and a second polyribonucleotide comprising the antisense strand, and wherein the cellular delivery module is covalently attached to the second polyribonucleotide.

61. The kit of claim **59**, wherein the cellular delivery module is attached to the RNA through a disulfide bond, or wherein the covalent attachment between the cellular delivery module and the RNA is reversible by exposure to light of a preselected wavelength.

62. The kit of claim **59**, wherein the cellular delivery module comprises a lipid or one or more myristoyl groups.

63. The kit of claim **57**, wherein the labeled RNA comprises one or more second caging groups associated with the cellular delivery module, the second caging groups inhibiting the cellular delivery module from mediating introduction of the labeled RNA into the cell.

64. The kit of claim **36**, wherein the kit comprises at least one buffer and/or at least one delivery reagent, wherein the delivery reagent can mediate introduction of the labeled RNA into the cell.

65. The kit of claim **64**, wherein the delivery reagent comprises a polypeptide, a PEP-1 peptide, an amphipathic peptide, an MPG^{ANLS} peptide, a cationic peptide, a homopolymer of D-arginine, a homopolymer of histidine, a homopolymer of lysine, or at least one lipid.

66. A kit for detecting a target mRNA in a cell, the kit comprising:

(a) a target RNA sensor, comprising

(i) a first RNA comprising at least one double-stranded region, the double-stranded region comprising a sense strand and an antisense strand, the antisense strand comprising a region which is substantially complementary to a region of a target mRNA, and

(ii) at least one first label, wherein initiation of RNA interference of the target mRNA by the first RNA in the cell results in an initiation-dependent change in a signal output of the first label; and,

(b) a reference RNA sensor, comprising

(i) a second RNA comprising at least one double-stranded region, the double-stranded region comprising a sense strand and an antisense strand, the antisense strand comprising a region which is substantially complementary to a region of a reference mRNA, and

(ii) at least one second label, wherein initiation of RNA interference of the reference mRNA by the second RNA in the cell results in an initiation-dependent change in a signal output of the second label; packaged in one or more containers.

67. The kit of claim **66**, wherein the signal output of the first label is detectably different from the signal output of the second label.

68. The kit of claim **66**, wherein the first label is a first fluorescent label, wherein the second label is a second fluorescent label, and wherein the initiation-dependent change in the signal output of the first and second label is a change in fluorescent emission.

69. The kit of claim **66**, comprising one or more of: instructions for using the target and reference RNA sensors to detect the presence of the target mRNA in the cell; instructions

for using the target and reference RNA sensors to quantitate an amount of the target mRNA present in the cell; a buffer; or a delivery reagent, wherein the delivery reagent can mediate introduction of the labeled RNA into the cell.

70. A composition, comprising: a population of labeled RNAs for detecting a target mRNA in a cell, each labeled RNA comprising:

an RNA comprising at least one double-stranded region, the double-stranded region comprising a sense strand and an antisense strand, the antisense strand comprising a region which is substantially complementary to a region of the target mRNA, and

at least one label, wherein the label is located a preselected position in the RNA, and wherein initiation of RNA interference of the target mRNA by the labeled RNA in the cell results in an initiation-dependent change in a signal output of the label.

71. The composition of claim **70**, wherein the label is a fluorescent label, and wherein the initiation-dependent change in the signal output of the label is a change in fluorescent emission.

72. The composition of claim **71**, wherein the labeled RNA comprises at least one quencher, wherein the label and the quencher are positioned in the RNA such that fluorescent emission by the label is quenched by the quencher, wherein initiation of RNA interference by the labeled RNA results in unquenching of the label, and wherein the initiation-dependent change in the signal output is an increase in the fluorescent emission by the label.

73. The composition of claim **71**, wherein the labeled RNA comprises two fluorescent labels, one being a donor and the other being an acceptor; wherein the donor and acceptor are positioned within the RNA such that energy transfer occurs between them; wherein initiation of RNA interference by the labeled RNA results in loss of energy transfer between the donor and the acceptor; and wherein the initiation-dependent change in the signal output is a decrease in fluorescent emission by the acceptor following excitation of the donor.

74. The composition of claim **70**, wherein the RNA comprises a first polyribonucleotide comprising the sense strand and a second polyribonucleotide comprising the antisense strand.

75. The composition of claim **74**, wherein the first polyribonucleotide comprises between 19 and 25 nucleotides, the second polyribonucleotide comprises between 19 and 25 nucleotides, and the double-stranded region comprises between 19 and 25 base pairs.

76. The composition of claim **75**, wherein the first polyribonucleotide and the second polyribonucleotide each comprise a two nucleotide TT 3' overhang, or wherein the first polyribonucleotide and the second polyribonucleotide form a duplex over their entire length.

77. The composition of claim **75**, wherein at least one caging group is covalently attached to a 5' hydroxyl or a 5' phosphate of the second polyribonucleotide.

78. The composition of claim **75**, wherein the label is a fluorescent label; wherein the labeled RNA comprises at least one quencher; wherein the label and the quencher are positioned in the RNA such that fluorescent emission by the label is quenched by the quencher; wherein initiation of RNA interference by the labeled RNA results in unquenching of the label; wherein the initiation-dependent change in the signal output is an increase in the fluorescent emission by the label; and wherein the label is attached to the first polyribonucleotide and the quencher is attached to the second polyribonucleotide, or the label is attached to the second polyribonucleotide and the quencher is attached to the first polyribonucleotide.

79. The composition of claim **78**, wherein:

one of the label and the quencher is located within three nucleotides of the 3' end of the first polyribonucleotide and the other of the label and the quencher is located within three nucleotides of the 3' end of the second polyribonucleotide;

one of the label and the quencher is located within three nucleotides of the 3' end of the first polyribonucleotide and the other of the label and the quencher is located within three nucleotides of the 5' end of the second polyribonucleotide;

one of the label and the quencher is located within three nucleotides of the 5' end of the first polyribonucleotide and the other of the label and the quencher is located within three nucleotides of the 3' end of the second polyribonucleotide;

one of the label and the quencher is located within three nucleotides of the 5' end of the first polyribonucleotide and the other of the label and the quencher is located within three nucleotides of the 5' end of the second polyribonucleotide;

one of the label and the quencher is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the first polyribonucleotide, and the other of the label and the quencher is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the second polyribonucleotide;

one of the label and the quencher is located within three nucleotides of the 5' end or the 3' end of the first or second polyribonucleotide and the other of the label and the quencher is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the opposite polyribonucleotide;

the label is attached at the 3' end of the first polyribonucleotide and the quencher is attached at the 3' end of the second polyribonucleotide;

the quencher is attached at the 3' end of the first polyribonucleotide and the label is attached at the 3' end of the second polyribonucleotide; or,

one of the label and the quencher is attached at the 5' end of the first polyribonucleotide and the other of the label and the quencher is attached at the 3' end of the second polyribonucleotide.

80. The composition of claim **75**, wherein the labeled RNA comprises two fluorescent labels, one being a donor and the other being an acceptor; wherein the donor and acceptor are positioned within the RNA such that energy transfer occurs between them; wherein initiation of RNA interference by the labeled RNA results in loss of energy transfer between the donor and the acceptor; and wherein the donor is attached to the first polyribonucleotide and the acceptor is attached to the second polyribonucleotide, or the donor is attached to the second polyribonucleotide and the acceptor is attached to the first polyribonucleotide.

81. The composition of claim **80**, wherein:

one of the donor and the acceptor is located within three nucleotides of the 3' end of the first polyribonucleotide and the other of the donor and the acceptor is located within three nucleotides of the 3' end of the second polyribonucleotide;

one of the donor and the acceptor is located within three nucleotides of the 3' end of the first polyribonucleotide and the other of the donor and the acceptor is located within three nucleotides of the 5' end of the second polyribonucleotide;

one of the donor and the acceptor is located within three nucleotides of the 5' end of the first polyribonucleotide and the other of the donor and the acceptor is located within three nucleotides of the 3' end of the second polyribonucleotide;

one of the donor and the acceptor is located within three nucleotides of the 5' end of the first polyribonucleotide and the other of the donor and the acceptor is located within three nucleotides of the 5' end of the second polyribonucleotide;

one of the donor and the acceptor is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the first polyribonucleotide, and the other of the donor and the acceptor is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the second polyribonucleotide;

one of the donor and the acceptor is located within three nucleotides of the 5' end or the 3' end of the first or second polyribonucleotide and the other of the donor and the acceptor is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the opposite polyribonucleotide;

the donor is attached at the 3' end of the first polyribonucleotide and the acceptor is attached at the 3' end of the second polyribonucleotide;

the acceptor is attached at the 3' end of the first polyribonucleotide and the donor is attached at the 3' end of the second polyribonucleotide; or,

one of the donor and the acceptor is attached at the 5' end of the first polyribonucleotide and the other of the donor and the acceptor is attached at the 3' end of the second polyribonucleotide.

82. The composition of claim **70**, wherein the RNA comprises a self-complementary polyribonucleotide.

83. The composition of claim **70**, wherein the double-stranded region comprises fewer than about 25 base pairs, fewer than about 30 base pairs, fewer than about 50 base pairs, fewer than about 80 base pairs, fewer than about 150 base pairs, fewer than about 250 base pairs, fewer than about 500 base pairs, fewer than about 1000 base pairs, or fewer than about 1500 base pairs.

84. The composition of claim **70**, wherein the labeled RNA comprises one or more first caging groups associated with the RNA, the first caging groups inhibiting the RNA from initiating RNA interference of the target mRNA in the cell.

85. The composition of claim **84**, wherein the first caging groups inhibit the RNA from initiating RNA interference of the target mRNA by at least about 30%, at least about 50%, at least about 75%, at least about 90%, at least about 95%, or at least about 98%, as compared to the RNA in the absence of the first caging groups, or wherein the first caging groups prevent the RNA from initiating RNA interference of the target mRNA.

86. The composition of claim **84**, wherein removal of or an induced conformational change in the first caging groups permits the RNA to initiate RNA interference of the target mRNA.

87. The composition of claim **84**, wherein the one or more first caging groups associated with the RNA are covalently attached to the RNA.

88. The composition of claim **87**, wherein the RNA comprises a first polyribonucleotide comprising the sense strand and a second polyribonucleotide comprising the antisense strand, and wherein the first caging group is covalently attached to the first polyribonucleotide and to the second polyribonucleotide.

89. The composition of claim **88**, wherein the first caging group is attached to the 3' end of the first polyribonucleotide and to the 5' end of the second polyribonucleotide.

90. The composition of claim **84**, wherein the one or more first caging groups are photoactivatable or photolabile.

91. The composition of claim **70**, wherein the labeled RNA comprises a cellular delivery module that can mediate introduction of the labeled RNA into the cell, the cellular delivery module being associated with the RNA, and wherein introducing the labeled RNA into the cell comprises contacting the cell with the labeled RNA associated with the cellular delivery module.

92. The composition of claim **91**, wherein the cellular delivery module comprises a polypeptide, a PEP-1 peptide, an amphipathic peptide, an MPG^{ANLS} peptide, a cationic peptide, a homopolymer of D-arginine, a homopolymer of histidine, a homopolymer of

lysine, a protein transduction domain, a protein transduction domain derived from an HIV-1 Tat protein, from a herpes simplex virus VP22 protein, from a Drosophila antennapedia protein, a model protein transduction domain, or a model protein transduction domain comprising a homopolymer of D-arginine.

93. The composition of claim **91**, wherein the cellular delivery module is covalently attached to the RNA.

94. The composition of claim **93**, wherein the RNA comprises a first polyribonucleotide comprising the sense strand and a second polyribonucleotide comprising the antisense strand, and wherein the cellular delivery module is covalently attached to the second polyribonucleotide.

95. The composition of claim **93**, wherein the cellular delivery module is attached to the RNA through a disulfide bond, or wherein the covalent attachment between the cellular delivery module and the RNA is reversible by exposure to light of a preselected wavelength.

96. The composition of claim **93**, wherein the cellular delivery module comprises a lipid or one or more myristoyl groups.

97. The composition of claim **91**, wherein the labeled RNA comprises one or more second caging groups associated with the cellular delivery module, the second caging groups inhibiting the cellular delivery module from mediating introduction of the labeled RNA into the cell.

98. The composition of claim **70**, comprising the target mRNA, a cell, a cell comprising the target mRNA, or a cell comprising the population.

99. A composition comprising:

(a) a target RNA sensor, comprising

(i) a first RNA comprising at least one double-stranded region, the double-stranded region comprising a sense strand and an antisense strand, the antisense strand comprising a region which is substantially complementary to a region of a target mRNA, and

(ii) at least one first label, wherein initiation of RNA interference of the target mRNA by the first RNA in the cell results in an initiation-dependent change in a signal output of the first label; and,

(b) a reference RNA sensor, comprising

(i) a second RNA comprising at least one double-stranded region, the double-stranded region comprising a sense strand and an antisense strand, the antisense strand comprising a region which is substantially complementary to a region of a reference mRNA, and

(ii) at least one second label, wherein initiation of RNA interference of the reference mRNA by the second RNA in the cell results in an initiation-dependent change in a signal output of the second label.

100. The composition of claim **99**, wherein the signal output of the first label is detectably different from the signal output of the second label.

101. The composition of claim **99**, comprising a cell, a cell comprising the target mRNA and/or the reference mRNA, or a cell comprising the target and the reference RNA sensors.

102. The composition of claim **99**, wherein the first label is a first fluorescent label, wherein the second label is a second fluorescent label, and wherein the initiation-dependent change in the signal output of the first and second label is a change in fluorescent emission.

103. A composition comprising a caged RNA, the caged RNA comprising:

an RNA comprising at least one double-stranded region, the double-stranded region comprising a sense strand and an antisense strand, the antisense strand comprising a region which is substantially complementary to a region of a target mRNA; and,

one or more first caging groups associated with the RNA, the first caging groups inhibiting the RNA from initiating RNA interference of the target mRNA in a cell comprising the caged RNA.

104. A composition comprising a caged RNA, the caged RNA comprising:

an RNA comprising a single polyribonucleotide strand comprising an antisense strand, the antisense strand comprising a region which is substantially complementary to a region of a target mRNA; and,

one or more first caging groups associated with the RNA, the first caging groups inhibiting the RNA from initiating RNA interference of the target mRNA in a cell comprising the caged RNA.

105. The composition of claim **103** or **104**, wherein the first caging groups inhibit the RNA from initiating RNA interference of the target mRNA by at least about 30%, at least about 50%, at least about 75%, at least about 90%, at least about 95%, or at least about 98%, as compared to the RNA in the absence of the first caging groups.

106. The composition of claim **103** or **104**, wherein the first caging groups prevent the RNA from initiating RNA interference of the target mRNA.

107. The composition of claim **103** or **104**, wherein removal of or an induced conformational change in the first caging groups permits the RNA to initiate RNA interference of the target mRNA.

108. The composition of claim **103**, wherein the RNA comprises a first polyribonucleotide comprising the sense strand and a second polyribonucleotide comprising the antisense strand.

109. The composition of claim **108**, wherein the first polyribonucleotide comprises between 19 and 25 nucleotides, the second polyribonucleotide comprises between 19 and 25 nucleotides, and the double-stranded region comprises between 19 and 25 base pairs.

110. The composition of claim **109**, wherein the first polyribonucleotide and the second polyribonucleotide each comprise a two nucleotide TT 3' overhang, or wherein the first polyribonucleotide and the second polyribonucleotide form a duplex over their entire length.

111. The composition of claim **109**, wherein at least one of the one or more first caging groups is covalently attached to a 5' hydroxyl or a 5' phosphate of the second polyribonucleotide.

112. The composition of claim **103**, wherein the RNA comprises a self-complementary polyribonucleotide.

113. The composition of claim **103**, wherein the double-stranded region comprises fewer than about 25 base pairs, fewer than about 30 base pairs, fewer than about 50 base pairs, fewer than about 80 base pairs, fewer than about 150 base pairs, fewer than about 250 base pairs, fewer than about 500 base pairs, fewer than about 1000 base pairs, or fewer than about 1500 base pairs.

114. The composition of claim **104**, wherein the polyribonucleotide strand comprises between 10 and 100 nucleotides, between 10 and 80 nucleotides, between 10 and 50 nucleotides, between 10 and 30 nucleotides, between 15 and 30 nucleotides, or between 19 and 25 nucleotides.

115. The composition of claim **104**, wherein at least one of the one or more first caging groups is covalently attached to a 5' hydroxyl or a 5' phosphate of the polyribonucleotide.

116. The composition of claim **103** or **104**, comprising the target mRNA, a cell, a cell comprising the target mRNA, or a cell comprising the caged RNA.

117. The composition of claim **103** or **104**, wherein the one or more first caging groups associated with the RNA are covalently attached to the RNA.

118. The composition of claim **103**, wherein the RNA comprises a first polyribonucleotide comprising the sense strand and a second polyribonucleotide comprising the antisense strand, and wherein the first caging group is covalently attached to the first polyribonucleotide and to the second polyribonucleotide.

119. The composition of claim **118**, wherein the first caging group is attached to the 3' end of the first polyribonucleotide and to the 5' end of the second polyribonucleotide.

120. The composition of claim **103** or **104**, wherein the one or more first caging groups are removable by sonication, photoactivatable, or photolabile.

121. The composition of claim **103** or **104**, wherein the one or more first caging groups each comprises a first binding moiety; the composition comprising a second binding moiety that can bind at least one of the first binding moieties.

122. The composition of claim **103**, wherein the RNA comprises at least one label, wherein initiation of RNA interference of the target mRNA by the labeled RNA in the cell results in an initiation-dependent change in a signal output of the label.

123. The composition of claim **122**, wherein the label is a fluorescent label, and wherein the initiation-dependent change in the signal output of the label is a change in fluorescent emission.

124. The composition of claim **123**, wherein the labeled RNA comprises at least one quencher, wherein the label and the quencher are positioned in the RNA such that fluorescent emission by the label is quenched by the quencher, wherein initiation of RNA interference by the labeled RNA results in unquenching of the label, and wherein the initiation-dependent change in the signal output is an increase in the fluorescent emission by the label.

125. The composition of claim **124**, wherein the RNA comprises a first polyribonucleotide comprising the sense strand and a second polyribonucleotide comprising the antisense strand; wherein the first polyribonucleotide comprises between 19 and 25 nucleotides, the second polyribonucleotide comprises between 19 and 25 nucleotides, and the double-stranded region comprises between 19 and 25 base pairs; and wherein the label is attached to the first polyribonucleotide and the quencher is attached to the second polyribonucleotide, or the label is attached to the second polyribonucleotide and the quencher is attached to the first polyribonucleotide.

126. The composition of claim **125**, wherein:

one of the label and the quencher is located within three nucleotides of the 3' end of the first polyribonucleotide and the other of the label and the quencher is located within three nucleotides of the 3' end of the second polyribonucleotide;

one of the label and the quencher is located within three nucleotides of the 3' end of the first polyribonucleotide and the other of the label and the quencher is located within three nucleotides of the 5' end of the second polyribonucleotide;

one of the label and the quencher is located within three nucleotides of the 5' end of the first polyribonucleotide and the other of the label and the quencher is located within three nucleotides of the 3' end of the second polyribonucleotide;

one of the label and the quencher is located within three nucleotides of the 5' end of the first polyribonucleotide and the other of the label and the quencher is located within three nucleotides of the 5' end of the second polyribonucleotide;

one of the label and the quencher is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the first polyribonucleotide, and the other of the label and the quencher is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the second polyribonucleotide;

one of the label and the quencher is located within three nucleotides of the 5' end or the 3' end of the first or second polyribonucleotide and the other of the label and the quencher is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the opposite polyribonucleotide;

the label is attached at the 3' end of the first polyribonucleotide and the quencher is attached at the 3' end of the second polyribonucleotide;

the quencher is attached at the 3' end of the first polyribonucleotide and the label is attached at the 3' end of the second polyribonucleotide; or,

one of the label and the quencher is attached at the 5' end of the first polyribonucleotide and the other of the label and the quencher is attached at the 3' end of the second polyribonucleotide.

127. The composition of claim **123**, wherein the labeled RNA comprises two fluorescent labels, one being a donor and the other being an acceptor; wherein the donor and acceptor are positioned within the RNA such that energy transfer occurs between them; wherein initiation of RNA interference by the labeled RNA results in loss of energy transfer between the donor and the acceptor; and wherein the initiation-dependent change in the signal output is a decrease in fluorescent emission by the acceptor following excitation of the donor.

128. The composition of claim **127**, wherein the RNA comprises a first polyribonucleotide comprising the sense strand and a second polyribonucleotide comprising the antisense strand; wherein the first polyribonucleotide comprises between 19 and 25 nucleotides, the second polyribonucleotide comprises between 19 and 25 nucleotides, and the double-stranded region comprises between 19 and 25 base pairs; and wherein the donor is attached to the first polyribonucleotide and the acceptor is attached to the second polyribonucleotide,

or the donor is attached to the second polyribonucleotide and the acceptor is attached to the first polyribonucleotide.

129. The composition of claim **128**, wherein:

one of the donor and the acceptor is located within three nucleotides of the 3' end of the first polyribonucleotide and the other of the donor and the acceptor is located within three nucleotides of the 3' end of the second polyribonucleotide;

one of the donor and the acceptor is located within three nucleotides of the 3' end of the first polyribonucleotide and the other of the donor and the acceptor is located within three nucleotides of the 5' end of the second polyribonucleotide;

one of the donor and the acceptor is located within three nucleotides of the 5' end of the first polyribonucleotide and the other of the donor and the acceptor is located within three nucleotides of the 3' end of the second polyribonucleotide;

one of the donor and the acceptor is located within three nucleotides of the 5' end of the first polyribonucleotide and the other of the donor and the acceptor is located within three nucleotides of the 5' end of the second polyribonucleotide;

one of the donor and the acceptor is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the first polyribonucleotide, and the other of the donor and the acceptor is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the second polyribonucleotide;

one of the donor and the acceptor is located within three nucleotides of the 5' end or the 3' end of the first or second polyribonucleotide and the other of the donor and the acceptor is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the opposite polyribonucleotide;

the donor is attached at the 3' end of the first polyribonucleotide and the acceptor is attached at the 3' end of the second polyribonucleotide;

wherein the acceptor is attached at the 3' end of the first polyribonucleotide and the donor is attached at the 3' end of the second polyribonucleotide; or,

one of the donor and the acceptor is attached at the 5' end of the first polyribonucleotide and the other of the donor and the acceptor is attached at the 3' end of the second polyribonucleotide.

130. The composition of claim **104**, wherein the RNA comprises at least one label, wherein initiation of RNA interference of the target mRNA by the labeled RNA in the cell results in an initiation-dependent change in a signal output of the label.

131. The composition of claim **103** or **104**, wherein the RNA is associated with a cellular delivery module that can mediate introduction of the RNA into a cell.

132. The composition of claim **131**, wherein the cellular delivery module comprises a polypeptide, a PEP-1 peptide, an amphipathic peptide, an MPG^{ΔNLS} peptide, a cationic peptide, a homopolymer of D-arginine, a homopolymer of histidine, a homopolymer of lysine, a protein transduction domain, a protein transduction domain derived from an HIV-1 Tat protein, from a herpes simplex virus VP22 protein, or from a Drosophila antennapedia protein, a model protein transduction domain, or a model protein transduction domain comprising a homopolymer of D-arginine.

133. The composition of claim **131**, wherein the cellular delivery module is covalently attached to the RNA.

134. The composition of claim **133**, wherein the cellular delivery module is attached to the RNA through a disulfide bond, or wherein the covalent attachment is reversible by exposure to light of a preselected wavelength.

135. The composition of claim **133**, wherein the cellular delivery module comprises a lipid or one or more myristoyl groups.

136. The composition of claim **131**, wherein the cellular delivery module is associated with one or more second caging groups which inhibit the cellular delivery module from mediating introduction of the RNA into a cell.

137. The composition of claim **103**, wherein the RNA comprises a first polyribonucleotide comprising the sense strand and a second polyribonucleotide comprising the antisense strand, and wherein a cellular delivery module is covalently attached to the second polyribonucleotide.

138. The composition of claim **103** or **104**, wherein the first caging group is a cellular delivery module.

139. The composition of claim **103** or **104**, wherein the caged RNA is bound to a matrix.

140. The composition of claim **139**, wherein the matrix is a surface, and the RNA is bound to the surface at a predetermined location within an array comprising other RNAs.

141. A kit for making the caged RNA of claim **103** or **104**, comprising an RNA, one or more first caging groups, and instructions for assembling the RNA and the first caging groups to form the caged RNA, packaged in one or more containers; or comprising one or more first caging groups and instructions for assembling the first caging groups and an RNA supplied by a user of the kit to form the caged RNA, packaged in one or more containers.

142. A kit for making the caged RNA of claim **122** or **130**, comprising one or more first caging groups, at least one label, and instructions for assembling the first caging groups, at least one label, and an RNA supplied by a user of the kit to form the caged RNA, packaged in one or more containers.

143. A method of selectively attenuating expression of a target gene in a cell, the method comprising:

introducing a caged RNA into the cell, the caged RNA comprising

(a) (i) an RNA comprising at least one double-stranded region, the double-stranded region comprising a sense strand and an antisense strand, the antisense strand comprising a region which is substantially complementary to a region of a target mRNA corresponding to the target gene,

or

(ii) an RNA comprising a single polyribonucleotide strand comprising an antisense strand, the antisense strand comprising a region which is substantially complementary to a region of a target mRNA corresponding to the target gene,

and

(b) one or more caging groups associated with the RNA, the caging groups inhibiting the RNA from initiating RNA interference of the target mRNA in the cell; and,

initiating RNA interference of the target mRNA by exposing the cell to uncaging energy, whereby exposure to the uncaging energy frees the RNA from inhibition by the caging groups.

144. The method of claim **143**, wherein exposing the cell to uncaging energy comprises exposing the cell to light of a first wavelength.

145. The method of claim **144**, wherein exposing the cell to light of the first wavelength comprises exposing the cell to light wherein intensity of the light and duration of exposure of the cell to the light are controlled such that a first portion of the caged RNA is uncaged and a second portion of the caged RNA remains caged.

146. The method of claim **145**, comprising exposing the cell to light of the first wavelength again.

147. The method of claim **145**, wherein the first portion is a selected amount.

148. The method of claim **143**, comprising contacting the cell and a test compound, and wherein the cell is exposed to the uncaging energy at a preselected time point with respect to a time at which the cell and the test compound are contacted.

149. The method of claim **143**, wherein the uncaging energy is directed at a preselected subset of a cell composition comprising the cell.

150. The method of claim **143**, wherein the caged RNA comprises a cellular delivery module that can mediate introduction of the caged RNA into the cell, the cellular delivery module being associated with the RNA, and wherein introducing the caged RNA into the cell comprises contacting the cell with the caged RNA associated with the cellular delivery module.

151. The method of claim **143**, wherein the RNA comprises at least one label, the method comprising detecting a signal from the label.

152. A composition, comprising:

a protein transduction domain covalently attached to an RNA; and,
the RNA, which RNA comprises:

- (a) at least one double-stranded region, the double-stranded region comprising a sense strand and an antisense strand, the antisense strand comprising a region which is substantially complementary to a region of a target mRNA, or
- (b) a single polyribonucleotide strand comprising an antisense strand, the antisense strand comprising a region which is substantially complementary to a region of a target mRNA corresponding to the target gene.

153. The composition of claim **152**, wherein the RNA of (a) comprises a first polyribonucleotide comprising the sense strand and a second polyribonucleotide comprising the antisense strand.

154. The composition of claim **153**, wherein the first polyribonucleotide comprises between 19 and 25 nucleotides, the second polyribonucleotide comprises between 19 and 25 nucleotides, and the double-stranded region comprises between 19 and 25 base pairs.

155. The composition of claim **154**, wherein at least one caging group is covalently attached to a 5' hydroxyl or a 5' phosphate of the second polyribonucleotide.

156. The composition of claim **152**, wherein the RNA of (a) comprises a self-complementary polyribonucleotide.

157. The composition of claim **152**, wherein the double-stranded region of the RNA of (a) comprises fewer than about 25 base pairs, fewer than about 30 base pairs, fewer than about 50 base pairs, fewer than about 80 base pairs, fewer than about 150 base pairs, fewer than about 250 base pairs, fewer than about 500 base pairs, fewer than about 1000 base pairs, or fewer than about 1500 base pairs; or, wherein the polyribonucleotide of (b) comprises between 10 and 100 nucleotides, between 10 and 80 nucleotides, between 10 and 50 nucleotides, between 10 and 30 nucleotides, between 15 and 30 nucleotides, or between 19 and 25 nucleotides.

158. The composition of claim **152**, comprising the target mRNA, a cell, a cell comprising the target mRNA, or a cell comprising the RNA.

159. The composition of claim **152**, comprising one or more first caging groups associated with the RNA, the first caging groups inhibiting the RNA from initiating RNA interference of the target mRNA in a cell.

160. The composition of claim **159**, wherein the one or more first caging groups associated with the RNA are covalently attached to the RNA.

161. The composition of claim **159**, wherein the one or more first caging groups are removable by sonication, photoactivatable, or photolabile.

162. The composition of claim **152**, wherein the protein transduction domain is derived from an HIV-1 Tat protein, from a herpes simplex virus VP22 protein, or from a Drosophila antennapedia protein, is a model protein transduction domain, or is a model protein transduction domain comprising a homopolymer of D-arginine.

163. The composition of claim **152**, wherein the protein transduction domain is attached to the RNA through a disulfide bond, or wherein the covalent attachment between the protein transduction domain and the RNA is reversible by exposure to light of a preselected wavelength.

164. The composition of claim **152**, comprising one or more second caging groups associated with the protein transduction domain, the second caging groups inhibiting the protein transduction domain from mediating introduction of the RNA into a cell.

165. The composition of claim **152**, wherein the RNA is bound to a matrix.

166. The composition of claim **165**, wherein the matrix is a surface, and the RNA is bound to the surface at a predetermined location within an array comprising other RNAs.

167. The composition of claim **152**, wherein the RNA comprises at least one label.

168. The composition of claim **167**, wherein initiation of RNA interference of the target mRNA by the RNA in a cell results in an initiation-dependent change in a signal output of the label.

169. The composition of claim **168**, wherein the label is a fluorescent label, and wherein the initiation-dependent change in the signal output of the label is a change in fluorescent emission.

170. The composition of claim **169**, wherein the RNA comprises at least one quencher, wherein the label and the quencher are positioned in the RNA such that fluorescent emission by the label is quenched by the quencher, wherein initiation of RNA interference by the RNA results in unquenching of the label, and wherein the initiation-dependent change in the signal output is an increase in the fluorescent emission by the label.

171. The composition of claim **169**, wherein the RNA comprises two fluorescent labels, one being a donor and the other being an acceptor; wherein the donor and acceptor are positioned within the RNA such that energy transfer occurs between them; and wherein initiation of RNA interference by the RNA results in loss of energy transfer between the donor and the acceptor.

172. A kit for making the composition of claim **152**, comprising an RNA, a protein transduction domain, and instructions for assembling the RNA and the protein transduction domain to form the composition, packaged in one or more containers; or comprising a protein transduction domain and instructions for assembling the protein transduction domain and an RNA supplied by a user of the kit to form the composition, packaged in one or more containers.

173. A method of introducing an RNA into a cell, the method comprising:

(a) providing a composition comprising

(i) an RNA comprising at least one double-stranded region, the double-stranded region comprising a sense strand and an antisense strand, the antisense strand comprising a region which is substantially complementary to a region of a target mRNA; or an RNA comprising a single polyribonucleotide strand comprising an antisense strand, the antisense strand comprising a region which is substantially complementary to a region of a target mRNA,

and

(ii) a protein transduction domain covalently attached to the RNA; and,

(b) contacting the composition and the cell, whereby the protein transduction domain mediates introduction of the RNA into the cell.

174. The method of claim 173, wherein the composition comprises one or more first caging groups associated with the RNA, the first caging groups inhibiting the RNA from initiating RNA interference of the target mRNA in the cell; the method comprising initiating RNA interference of the target mRNA by exposing the cell to uncaging energy of a first type, whereby exposure to the uncaging energy frees the RNA from inhibition by the first caging groups.

175. The method of claim 174, wherein exposing the cell to uncaging energy of the first type comprises exposing the cell to light of a first wavelength.

176. The method of claim 173, wherein the protein transduction domain is derived from an HIV-1 Tat protein, from a herpes simplex virus VP22 protein, or from a Drosophila antennapedia protein, is a model protein transduction domain, or is a model protein transduction domain comprises a homopolymer of D-arginine.

177. The method of claim 173, wherein the protein transduction domain is covalently attached to the RNA through a disulfide bond; or wherein the covalent attachment between the protein transduction domain and the RNA is reversible by exposure to light of a preselected wavelength, the method comprising exposing the cell to light of the preselected wavelength.

178. The method of claim 173, wherein the composition comprises one or more second caging groups associated with the protein transduction domain, the second caging groups inhibiting the protein transduction domain from mediating introduction of the RNA into the cell; the method comprising initiating introduction of the RNA into the cell by exposing the composition to uncaging energy of a second type, whereby exposure to the uncaging energy frees the protein transduction domain from inhibition by the second caging groups.

179. The method of claim 173, wherein the RNA comprises at least one label, the method comprising detecting a signal from the label.

180. A composition, comprising:

an RNA comprising at least one double-stranded region, the double-stranded region comprising a sense strand and an antisense strand, the antisense strand comprising a region which is substantially complementary to a region of a target mRNA; or an RNA comprising a single polyribonucleotide strand comprising an antisense strand, the antisense strand comprising a region which is substantially complementary to a region of a target mRNA;

and,

a lipid covalently attached to the RNA.

181. The composition of claim **180**, wherein the lipid comprises a fatty acid or a myristoyl group.

182. The composition of claim **180**, wherein the lipid is covalently attached to the RNA through a disulfide bond, or wherein the covalent attachment between the lipid and the RNA is reversible by exposure to light of a preselected wavelength.

183. The composition of claim **180**, comprising the target mRNA, a cell, a cell comprising the target mRNA, or a cell comprising the RNA.

184. A method of introducing an RNA into a cell, the method comprising:

(a) providing a composition comprising

(i) an RNA comprising at least one double-stranded region, the double-stranded region comprising a sense strand and an antisense strand, the antisense strand comprising a region which is substantially complementary to a region of a target mRNA; or an RNA comprising a single polyribonucleotide strand comprising an antisense strand, the antisense strand comprising a region which is substantially complementary to a region of a target mRNA;

and,

(ii) a lipid covalently attached to the RNA; and,

(b) contacting the composition and the cell, whereby the lipid mediates introduction of the RNA into the cell.

185. The method of claim **184**, wherein the lipid comprises a fatty acid or a myristoyl group.

186. The method of claim **184**, wherein the lipid is covalently attached to the RNA through a disulfide bond; or wherein the covalent attachment between the lipid and the RNA is reversible by exposure to light of a preselected wavelength, the method comprising exposing the cell to light of the preselected wavelength.

187. A composition, comprising:

one or more vectors that comprise or encode an RNA comprising at least one double-stranded region, the double-stranded region comprising a sense strand and an antisense strand, the antisense strand comprising a region which is substantially complementary to a region of a target mRNA; and,

a caged first activation component, comprising one or more caging groups associated with a first activation component, which first activation component directly or indirectly increases expression of the RNA from the one or more vectors in a cell comprising the one or more vectors and the first activation component, and which one or more caging groups inhibit the first activation component from increasing expression of the RNA in the cell.

188. The composition of claim **187**, comprising a second activation component, which second activation component directly increases expression of the RNA when bound by the first activation component.

189. The composition of claim **188**, wherein the first activation component comprises tetracycline.

190. The composition of claim **187**, comprising a third activation component, which third activation component directly increases expression of the RNA when indirectly activated by the first activation component.

191. The composition of claim **190**, wherein the first activation component comprises IP3 or Ca^{2+} and the third activation component comprises an NF-AT transcription factor complex.

192. The composition of claim **187**, comprising the target mRNA, a cell, a cell comprising the target mRNA, or a cell comprising the one or more vectors and the caged first activation component.

193. The composition of claim **187**, wherein the RNA comprises a first polyribonucleotide comprising the sense strand and a second polyribonucleotide comprising the antisense strand, or wherein the RNA comprises a self-complementary polyribonucleotide.

194. The composition of claim **187**, wherein the one or more first caging groups are removable by sonication, photoactivatable, or photolabile.

195. The kit comprising the components of the composition of claim **187**, and optionally comprising a vector that comprises or encodes a second or a third activation component; packaged in one or more containers.

196. A method of selectively attenuating expression of a target mRNA in a cell, the method comprising:

introducing one or more vectors that comprise or encode an RNA comprising at least one double-stranded region, the double-stranded region comprising a sense strand and an antisense strand, the antisense strand comprising a region which is substantially complementary to a region of the target mRNA;

introducing a caged first activation component into the cell, wherein the caged first activation component comprises one or more caging groups associated with a first activation component, which first activation component directly or indirectly increases expression of the RNA from the one or more vectors, and which one or more caging groups inhibit the first activation component from increasing expression of the RNA; and,

exposing the cell to uncaging energy, whereby exposure to the uncaging energy frees the first activation component from inhibition by the caging groups, resulting in increased expression of the RNA.

197. The method of claim **196**, wherein the first activation component indirectly increases expression of the RNA by binding to a second activation component, whereby the bound second activation component directly increases expression of the RNA.

198. The method of claim **197**, wherein the first activation component comprises tetracycline.

199. The method of claim **196**, wherein the first activation component indirectly increases expression of the RNA by indirectly activating a third activation component, whereby the activated third activation component directly increases expression of the RNA.

200. The method of claim **199**, wherein the first activation component comprises IP3 or Ca²⁺ and the third activation component comprises an NF-AT transcription factor complex.

201. The method of claim **196**, wherein exposing the cell to uncaging energy comprises exposing the cell to light of a first wavelength.

202. A method of selectively attenuating expression of a target gene in a cell, the method comprising:

introducing a first caged DNA and a second caged DNA into the cell, the first caged DNA comprising a first DNA encoding an RNA sense strand and one or more caging groups associated with the first DNA, the second caged DNA comprising a second DNA encoding an RNA antisense strand and one or more caging groups associated with the second DNA, the caging groups inhibiting transcription of the first and second DNAs, the first and second DNAs each comprising at least a portion of the target gene, and the sense and antisense strands being at least partially complementary and able to form a duplex over at least a portion of their lengths; and,

initiating RNA interference by generating double-stranded RNA by exposing the cell to uncaging energy, whereby exposure to the uncaging energy frees the first and second DNAs from inhibition by the caging groups and permits transcription of the first and second DNAs to occur.

203. The method of claim **202**, wherein the sense strand comprises a first polyribonucleotide and the antisense strand comprises a second polyribonucleotide, or wherein the sense and antisense strands comprise a single, self-complementary polyribonucleotide.

204. The method of claim **202**, wherein exposing the cell to uncaging energy comprises exposing the cell to light of a first wavelength.